

**Translation**

**PATENT COOPERATION TREATY**

**PCT**

**INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY**  
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>20040483</b>	<b>FOR FURTHER ACTION</b>	See Form PCT/IPEA/416
International application No. <b>PCT/ES2004/000361</b>	International filing date ( <i>day/month/year</i> ) <b>04.08.2004</b>	Priority date ( <i>day/month/year</i> ) <b>04.08.2003</b>
International Patent Classification (IPC) or national classification and IPC <b>A61K31/675, 31/185, 31/53, A61P25/28</b>		
Applicant <b>UNIVERSIDAD DEL PAIS VASCO - EUSKAL HERRIKO UNIBERTSITATEA</b>		

<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of _____ sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input checked="" type="checkbox"/> (sent to the applicant and to the International Bureau) a total of <u>1</u> sheets, as follows:</p> <p><input checked="" type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>																									
<p>4. This report contains indications relating to the following items:</p> <table><tr><td><input checked="" type="checkbox"/></td><td>Box No. I</td><td>Basis of the report</td></tr><tr><td><input type="checkbox"/></td><td>Box No. II</td><td>Priority</td></tr><tr><td><input type="checkbox"/></td><td>Box No. III</td><td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td></tr><tr><td><input type="checkbox"/></td><td>Box No. IV</td><td>Lack of unity of invention</td></tr><tr><td><input checked="" type="checkbox"/></td><td>Box No. V</td><td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td></tr><tr><td><input type="checkbox"/></td><td>Box No. VI</td><td>Certain documents cited</td></tr><tr><td><input type="checkbox"/></td><td>Box No. VII</td><td>Certain defects in the international application</td></tr><tr><td><input type="checkbox"/></td><td>Box No. VIII</td><td>Certain observations on the international application</td></tr></table>		<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input type="checkbox"/>	Box No. II	Priority	<input type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input type="checkbox"/>	Box No. VIII	Certain observations on the international application
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Date of submission of the demand	Date of completion of this report																								
Name and mailing address of the IPEA/ES	Authorized officer																								
Facsimile No.	Telephone No.																								

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

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Box No. I	Basis of the report
1.	<p>With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.</p> <p><input type="checkbox"/> This report is based on translations from the original language into the following language _____, which is the language of a translation furnished for the purposes of:</p> <p><input type="checkbox"/> international search (Rule 12.3 and 23.1(b))</p> <p><input type="checkbox"/> publication of the international application (Rule 12.4)</p> <p><input type="checkbox"/> international preliminary examination (Rule 55.2 and/or 55.3)</p> <p>2. With regard to the elements of the international application, this report is based on <i>(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)</i>:</p> <p><input type="checkbox"/> the international application as originally filed/furnished</p> <p><input checked="" type="checkbox"/> the description:</p> <p>pages <u>1-23</u> _____ as originally filed/furnished</p> <p>pages* _____ received by this Authority on _____</p> <p>pages* _____ received by this Authority on _____</p> <p><input checked="" type="checkbox"/> the claims:</p> <p>nos. _____ as originally filed/furnished</p> <p>nos.* _____ as amended (together with any statement) under Article 19</p> <p>nos.* <u>24</u> _____ received by this Authority on <u>26.09.2005</u></p> <p>nos.* _____ received by this Authority on _____</p> <p><input checked="" type="checkbox"/> the drawings:</p> <p>sheets <u>1-9</u> _____ as originally filed/furnished</p> <p>sheets* _____ received by this Authority on _____</p> <p>sheets* _____ received by this Authority on _____</p> <p><input type="checkbox"/> a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.</p> <p>3. <input type="checkbox"/> The amendments have resulted in the cancellation of:</p> <p><input type="checkbox"/> the description, pages _____</p> <p><input type="checkbox"/> the claims, nos. _____</p> <p><input type="checkbox"/> the drawings, sheets/figs _____</p> <p><input type="checkbox"/> the sequence listing (<i>specify</i>): _____</p> <p><input type="checkbox"/> any table(s) related to sequence listing (<i>specify</i>): _____</p> <p>4. <input type="checkbox"/> This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).</p> <p><input type="checkbox"/> the description, pages _____</p> <p><input type="checkbox"/> the claims, nos. _____</p> <p><input type="checkbox"/> the drawings, sheets/figs _____</p> <p><input type="checkbox"/> the sequence listing (<i>specify</i>): _____</p> <p><input type="checkbox"/> any table(s) related to sequence listing (<i>specify</i>): _____</p> <p>* If item 4 applies, some or all of those sheets may be marked "superseded."</p>

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement		
1. Statement			
Novelty (N)	Claims		YES
	Claims	1, 2, 5, 6	NO
Inventive step (IS)	Claims		YES
	Claims	1, 2, 5, 6	NO
Industrial applicability (IA)	Claims	1-6	YES
	Claims		NO
2. Citations and explanations (Rule 70.7)			
Documents taken into consideration:			
D1: WO 99/38532 A 05.08.1999			
D2: British Journal of Pharmacology, vol. 120, pages 954-960. 1997			
D3: Journal of Neurosurgery, vol 07, pages 129-135. 2002			
D4: Pain, vol. 96, pages 99-105 2002			
D5: Pain, vol. 96, pages 99-105 2000			
D6: WO 98/03178 A 29.01.1998			
D7: EP 1 310 493 A 14.05.2003			
D8: WO 03/047515 A 12.06.2003			
<p>The present invention relates to antagonists of purinergic receptor P2X7, selected from Evans Blue, NF279, BBG, o-ATP, KN62, TNP-ATP and HMA, pharmaceutical compositions containing same and the use thereof for treating demyelinating and auto-immune diseases, preferably multiple sclerosis.</p>			
<p>Documents D1 to D5 relate to various purinergic receptor antagonists such as NF23, suramin, Evans Blue, Trypan Blue, DIDS, PPADS and TNP-ATP, having pharmacological applications such as the prevention of fibrosis and</p>			

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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Box No. V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement

sclerosis, vasoconstrictive response antagonism, vasospasm reversion, abdominal pain reduction and allodynia control. Document D6 relates to the use of P2Y receptor antagonists, particularly P2Y<sub>1</sub> receptor antagonists, such as suramin, PPADS and DIDS, for the treatment of demyelinating diseases, including multiple sclerosis. Documents D7 and D8 relate to compounds having P2X<sub>7</sub> purinergic receptor antagonist activity and the use thereof for treating auto-immune, inflammatory or degenerative diseases. The compounds are derived from adamantane and L-tyrosine derivatives.

Claims 1, 2, 5 and 6 relate to products (compounds or compositions) defined in terms of the mode of action and therapeutic use thereof. Such reference to the use of the products is considered to be a mere description constituting a technical feature that has no limiting effect for the purposes of assessing the novelty of said claims. Given that the compounds set forth in claims 1 and 2 are known from the prior art, and the P2X receptor antagonist activity thereof has already been disclosed, the above-mentioned product claims cannot be considered novel or inventive (PCT Article 33(2) and (3)).

As regards claims 3 and 4 relating to the use of said products, none of the cited documents describes the use of said products in the treatment of demyelinating and auto-immune diseases, preferably multiple sclerosis. As a result, the subject matter of claims 3 and 4 is considered to be novel and to involve an inventive step (PCT Article 33(2) and (3)).